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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,169	11/28/2005	Roger R. C. New	117-565	7760

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EXAMINER	
HA, JULIE	
ART UNIT	PAPER NUMBER
1654	
MAIL DATE	DELIVERY MODE
06/08/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	Application No.	Applicant(s)	
	10/553,169	NEW, ROGER R. C.	
	Examiner	Art Unit	
	JULIE HA	1654	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 01 May 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.
   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *1,2,5-7,9-14,19-24,26-38*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See continuation of 11 below.
12. ☒ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). 5/1/2009
13. ☐ Other: _____.

/Cecilia Tsang/
Supervisory Patent Examiner, Art Unit 1654

Claims 9-11 and 19-21 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite, for the reasons set forth in the previous office action.

Applicant argues that analogues and derivatives of calcitonin, growth hormone, and calcitonin are a matter of public record. Applicant indicates Merck index in regards to PTH, calcitonin, and growth hormone. Applicant further submitted definitions of derivative and analogs, and indicates that "derivative" contains esential elements of the parent compound, and an "analogue" is a structural derivative, often differing by just a single element."

Applicant's arguments have been fully considered but have not been found persuasive. As indicated in the office action, there are vast numbers of different growth hormones that have different amino acid content. PTH also has multiple sequences. For example, GenBank No. AAA72739 disclose a 144 amino acid residue sequence. A derivative or an analog of the parent PTH sequence can be any sequence variance of thie wildtype, any addition, deletion or substitution or any mutation of the sequence, including non-natural amino acids. In regards to the Merck index, these do not indicate what derivatives and analogs of, for example PTH, are encompasses within "derivative and analogues thereof, either synthetic or from natural souces, conforming to structures derived from either human or animal origin, or is single, double or triple-stranded RNA".

Claims 9-11 and 19-21 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for the reasons set forth in the previous office action.

Applicant argues that "the analogues and derivatives of the macromolecules are a matter of public record…the calculation is believed to be misleading. Independent claims 1 and 26 require the macromolecule to be active, and so only active derivatives and analogues would be covered by claims 9-11 and 19-21. Only a small fraction of the huge number of alleged derivatives contemplated by the Examiner would be active." Applicant futher argues that "nearly all of the polypeptides included in the Examiner's calculation have not even a single residue in common with human calcitonin and so cannot be considered to be analogues or derivatives of it." Applicant further argues that "the USPTO has routinely granted US patents for applications with claims containing references to "analogues" and "derivatives" of active macromolecules."

Applicant's arguments have been fully considered but have not been found persuasive. As dexcribed in the previous office action, human calcitonin has 93 amino acid residues. Since there are 93 residues and 20 naturally occurring amino acids that can be substituted for the 93 amino acid residues, there are 2.3 x 10^39 different possibilities. These would have different variations of the parent residue, with each and every residue that are substituted with the 20 naturally occurring amino acids. For example, the first residue will be substituted with all 20 naturally occurring amino acids while the 92 residues remain the same, leading to 20 different possible sequences of calcitonin. The calculation encompasses all possible variation of human calcitonin. Furthermore, when non-natural amino acids are factored into the equation, the numbers are innumerable. Further, for any single, double or triple-stranded RNA, this can have varying sequences, lengths and characteristics. Therefore, the numbers of possibilities of derivatives, analogs or sequence variants of the polypeptides and RNA sequences would increase according to the number of residues of that particular polypeptide or RNA sequence. In regards to Applicant's arguments that "the USPTO has routinely granted US patents for applications with claims containing references to "analogues" and "derivatives"' each case is examined on its own merits. Therefore, the rejection is maintained.

Claims 1-2, 5-7, 9-14 and 26-38 remain rejected under 35 U.S.C. 103(a) as being unpatentable over New (US Patent No. 5,853,748) in view of Desai (US Patent No. 5,206,219) and Sonnenberg & Kotchen (Curr. Op. Neph. Hyperten., 1998), for the reasons set for th in the previous office action.

Applicant argues that " claim 26 does recite the effect of the PG/BHA, thus, claim 26 does require the effect to be realized." Further, Applicant argues that "composition claim 38 has now been amended to specify that the composition is an oral pharmaceutical composition….destined to be administered orally, and so will inevitably entail realization of the effect of the PG/BHA." Applicant argues that "all antioxidants and preservatives are not compatible" Further, Applicant argues that "bicarbonate is known as a strong buffer at its buffering pH (7-9), and by definition, it would require a large amount of acid to change the pH significantly." Applicant directes the Examiner to Example 6, "which gives in vivo data to prove the superior efficacy of compositions wherein an additive as defined in claim 1 is present."

In the 132 declaration, Applicant argues that "Applicant conducted experiments to investigate whetehr or not it is actually possible to prepare a clare aqueous solution containing, along with chenodeoxycholate, both (i) sodium bicarbonate, and (ii) either PG or BHA." Applicant aruges that "a turbid dispersion was formed and even after incubation at 60C, it was still not possible to achieve a clear aqueous solution. Upon continued incubation for one hour at 37C, the mixture remained cloudy…the mixture without sodium bicarbonate formed a completely clear solution."

Applicant's arguments have been fully considered but have not been found persuasive. In regards to claim 26, the combined prior art encompasses all of the active method steps of instant claim, therefore, when the pharmaceutical composition is administered to a patient, the effect would occur, therefore, the effect is realized. In regards to Applicant's argument that "not all antioxidants and preservatives are not compatible", the claims do not recite that these components need to be compatible. The claim recites, "A pharmaceutical composition comprising a mixture of (a) an active macromolecule principle, (b) a non-conjugated bile acid or salt, and (c) an additive chosen from (i), (ii) or (iii)." New also teaches oral pharmaceutical composition. The New reference teaches that "bile salts start to be converted to their conjugate acid at pH of about 6.8 or below and the acid form is insoluble in aqueous solutions," therefore, it would have been obvious to one of ordinary skill in the art to maintain the pH of the intestinal fluid in between pH 6.8 and 7.5. New reference teaches that the pH of the gut is between 5 to 7, therefore, one would have been motivated to maintain the pH of about 7, which includes 7.5. It would not take a lot of other agents to lower the pH from 8-8.5 to 6.8-7.5.

The declaration was not persuasive. The instant claim 1 does not recite that the pharmaceutical composition must be in a clear

solution. Furthermore, the specific concentration is not a limitation of the claims. At a lower concentration, the sodium bicarbonate, bile acid or salt, and PG/BHA may be soluble. A pharmaceutical composition can be in a form of emulsion, insouble mixture, a cloudy suspension, capsulre, dispersion, micropartilce dispersion and so on. .

Conclusion

No claim is allowed.
Any inquiry concerning this communication or earlier communications from the examiner should be directed to JULIE HA whose telephone number is (571)272-5982. The examiner can normally be reached on Mon-Thurs, 5:30 AM to 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.